A particulate guaifenesin composition, comprising particles that comprise an agglomerated mixture of guaifenesin particles and a polyvinylpyrrolidone binder, wherein the composition comprises from about 85 percent by weight to about 97.5 percent by weight guaifenesin and wherein by sieve analysis, based on the total weight of the composition, less than about 30 percent by weight of the particles of the composition exhibit a particle size of greater than about 425 micrometers and greater than about 80 percent by weight of the particles of the composition exhibit a particle size of greater than about 45 micrometers.

Applicant's claim 31 is directed to:

A guaifenesin composition, comprising guaifenesin particles, a polyvinylpyrrolidone binder, and a solubilizer, or a disintegrant, or a solubilizer and a disintegrant, wherein the composition comprises from about 85 percent by weight to about 97.5 percent by weight guaifenesin, and is in the form of particles, said particles of said composition comprising particles that comprise an agglomerated mixture of guaifenesin particles and polyvinylpyrolidone binder, wherein the composition is capable of being compressed into a compressed dosage form without addition of other components, and wherein by sieve analysis, based on the total weight of the composition, less than about 30 percent by weight of the particles exhibit a particle size of greater than about 425 micrometers and greater than about 80 percent by weight of the particles exhibit a particle size of greater than about 45 micrometers.

II. Rejection Under 35 USC § 103

Claims 1-4, 6-8, 31 and 33-36 are rejected under 35 U.S.C. 103(a) as being unpatentable over US 4,798,725 to Patel (Patel).

II.A. Patel

Patel is directed to capsule for oral administration, comprising a capsule shell and the particulate mixture of Patel within the shell (see col. 2, lines 63-66 of Patel). The particulate mixture comprises a particles of an active drug ingredient, particles of polyvinylpyrrolidone, and particles of a carboxyvinylpolymer (see col. 3, lines 13-18 of Patel), is made by simply dry blending the particulate ingredients (col. 8, lines 13-17 of Patel), and is "flowable" (see col. 2, line 66 to col. 3, line 13 of Patel). Guaifenesin is suitable as the active drug ingredient (see col. 6, line 32 and Col. 13, Example 7 of Patel). The polyvinylpyrrolidone component of the mixture of Patel is present as a "necessary ingredient to achieve sustained release of the active drug ingredient" (see col. 3, lines 41- 44 of Patel) via formation of a cohesive mass upon being wetted by gastrointestinal juice when the capsule of Patel is permeated by such juice after oral administration (see col. 3, line 63-col.4, line 9 of Patel).

II.B.. Physical Form

As acknowledged by the examiner, Patel does not teach particles that comprise an agglomerated mixture of guaifenesin and polyvinylpyrrolidone, as required by Applicant's claims 1 and 31. In contrast, the particulate mixture of Patel is disclosed as a simple mixture made by dry blending of particulate ingredients (col. 8, lines 13-17 of Patel).

Applicant submits that Patel discloses use of polyvinylpyrrolidone as a sustained release agent, does not disclose, suggest, or provide any motivation for use of polyvinylpyrrolidone as a binder, and does not disclose, suggest, or provide any motivation for making particles that comprise an agglomerated mixture of guaifenesin and polyvinylpyrrolidone, as required by Applicant's claims 1 and 31.

II.C. Particle size

As acknowledged by the examiner, Patel does not teach the exact percentages of the particles of specific sizes claimed by Applicant. However, the examiner states that Patel teaches that the particles have a size such that they pass through 60 mesh, which according to the instant specification is 250 microns, and thus is within the claimed range. The examiner observes that according to claim 1 of the present application, < 30% of the particles have a size greater than 425 microns and >80% of the particles have a size greater than 45 microns and urges that the size of the instant particles is therefore between 45 and 425 microns, which includes 250 microns

Applicant submits that Patel provides no disclosure regarding the particle size distribution of the particulate mixture of Patel. Applicant points out that the particle size described by Patel refers only to the particle size of the polyvinylpyrrolidone component of the mixture of Patel (see col. 4, lines 17-20 of Patel), does not refer to the particle size of the particulate mixture of Patel, and is not adequate to characterize the particle size distribution of the particulate mixture of Patel.

Applicant further submits that Patel's teaches that the preferred polyvinlypyrrolidone particles have a size such that they pass through 60 mesh does not establish that such particles are within the range of particle sizes claimed in Applicant's claims 1 and 31. Patel's expressed preference that the

particle size of the polyvinylpyrrolidone component of Patel's mixture is such that 100 percent of the particles will pass through a 60 mesh sieve establishes only that the preferred polyvinylpyrrolidone particles are less than 250 micrometers in size, and does not disclose or in any way suggest that the preferred polyvinylpyrrolidone particles meet the limitation of Applicant's claims requiring that greater than about 80 percent by weight of the particles of the claimed composition exhibit a particle size of greater than 45 micrometers. For example, polyvinylpyrrolidone particles having a particle size distribution wherein 100 percent by weight of the particles have a particles size of less than 45 micrometers would satisfy Patel's preference for polyvinylpyrrolidone particles that pass through a 60 mesh screen, but would not satisfy the limitation of Applicant's claims requiring that greater than about 80 percent by weight of the particles of the claimed composition exhibit a particle size of greater than 45 micrometers.

Applicant further submits that, in any case, the particle size distribution of the polyvinylpyrrolidone component of the particulate mixture of Patel is not relevant to the particle size distribution of the Applicant's claimed particles which, as discussed above, must comprise an agglomerated mixture of guaifenesin particles and polyvinylpyrrolidone.

The examiner further acknowledges that Patel does not teach the flow rate claimed by Applicant. Applicant points out that Patel does not disclose any information, other than the above discussed observation that the particulate mixture of Patel is flowable, regarding the flow rate of the particulate mixture of Patel.

Applicant further submits that since the disclosure of Patel is deficient in respect to both the particle size distribution of the particulate mixture of Patel and the flow rate of the particulate mixture of Patel, it can provide no basis for one of ordinary skill to predict the flow rate of the particulate mixture of Patel, or to

correlate changes in flow rate with changes in the particle size distribution of the particulate mixture of Patel.

II.D. Relative Composition

The examiner acknowledges that Patel does not disclose:

- percentages of the amounts of guaifenesin, and
- specific solubilizer maltodextrin,

but observes that Patel also suggests addition of the pharmaceutical excipients such as silicon dioxide, stearic acid, talc and other conventional additives (col. 7).

Applicant submits that Patel provides no disclosure or suggestion that would have led one of ordinary skill in the art to obtain Applicant's claimed composition by modifying the amounts of various components of the particulate mixture of Patel. This distinction is even clearer with respect to the directly compressible composition claimed in Applicant's 31-36, since the performance requirements for the claimed composition, which is suitable for being directly compressed into self-supporting tablets, would be different than those for those of Patel's composition, which is to be packed into capsule shells.

III. Conclusion

The examiner concludes that it would have been obvious that one of an ordinary skill in the art at the time of the instant invention to optimize the amounts of particulate guaifenesin, PVP and other additives, and choose the particle sizes and the excipients in the composition of Patel, so as to achieve the desired flow rate of the particle mixture (of active and the excipients) and thus achieve a desired release pattern.

Applicant submits that the examiner's conclusion completely neglects Applicant's limitation requiring particles that comprise an agglomerated mixture of guaifenesin particles and polyvinylpyrrolidone.

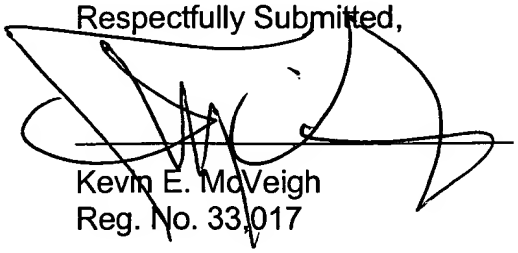
Applicant further submits that submits that the examiners conclusion regarding optimization of the relative amounts of ingredients and selection of the particle size of to achieve a desired flow rate of the particle mixture is flawed in that, for the reasons discussed above, is not supported by the disclosure of Patel.

Applicant urges that one of ordinary skill in the art skill would not have found the present invention obvious in view of Patel, because Patel does not disclose or suggest:

- particles that comprise an agglomerated mixture of guaifenesin particles and polyvinylpyrrolidone, as required by the claims of the present application, or
- the relative composition of Applicant's claimed composition, or
- the particle size distribution of Applicant's claimed composition.

For all the reasons discussed above, Applicant submits that all claims pending in the present application are in now condition for allowance and therefore requests that the Examiner issue a *Notice of Allowance* for claims 1-4, 6-8, 31 and 33-36 in the present application.

Respectfully Submitted,



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